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identical peptide insert (SEQ ID NO: 39) previously described in rat and human trkA (Barker, *et al.*, supra).

Please replace page 118 with the attached replacement page 118, captioned "REPLACEMENT SHEET." A marked up version of page 118 as originally filed is enclosed and captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Please further amend the specification by entering the attached Sequence Listing following the Abstract on page 120.

Remarks

Original Figures 1 and 2 have been amended to clearly identify the two separate sequences shown as "1A", "1B", and "2A" and "2B", respectively. Corresponding amendments have been made in the legends of Figures 1 and 2. These changes are of formal nature, and do not add new matter into the specification.

Similar to amendments made in the parents of the present application, a substitute Figure 4 is submitted that contains an explanation of each symbol used in the schematic representation of the trks and their alternate splice forms and their domains. In addition, the legend of Figure 4 has been amended to better describe Figure 4 by defining the meaning of the triangles, which represent optionally present peptide inserts. Support for these changes is found most notably in the specification at page 17, line 1 to page 18, line 8, where the trk domains are described, in the detailed description of the trk's and their alternate splicing forms at pages 97-103, in the Examples at page 98, lines 22-28, where the 6 amino acid peptide insert into trkA is described by means of its nucleic acid sequence, and in the description of the non-human trkB isoform at page 98, line 30 to page 99, line 11.

In order to ensure conformity with the Sequence Listing submitted concurrently herewith, amendments to the specification have been made to reflect the new SEQ ID Nos. The Sequence Listing is believed to better organize the sequences than the original SEQ ID Nos. For the Examiner's convenience, a brief explanation of the SEQ ID NO changes follows. SEQ ID NO: 1 remains the nucleic acid sequence for a full-length human trkB; however, SEQ ID NO: 2 is now the translated amino acid sequence of SEQ ID NO: 1. SEQ ID NO: 3 is a truncated human trkB

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nucleic acid sequence, and SEQ ID NO: 4 is its corresponding translated amino acid sequence, which finds support in Figure 1B and in the detailed description of this splice form in the specification. SEQ ID NO: 5 is a full-length human trkC nucleic acid sequence (originally SEQ ID NO: 2), and SEQ ID NO: 6 is its corresponding translated amino acid sequence, which is also supported in Figure 2A. SEQ ID NO: 7 is a truncated human trkC nucleic acid sequence, and SEQ ID NO: 8 is its corresponding amino acid sequence, which finds support in Figure 2B and in the detailed description of this splice form in the specification. SEQ ID NO: 9 is a full-length human trkA amino acid sequence, which is found in Figure 16. SEQ ID NOS: 10 through 35 are nucleic acid sequences for the oligonucleotides found in Table 1. SEQ ID NO: 36 is amino acid sequence ESTDNFILF, which is bracketed in Figure 2A. SEQ ID NO: 37 is amino acid sequence LFNPSGNDFCIWCE, which is also bracketed in Figure 2A. SEQ ID NO: 38 is the nucleic acid sequence TCTCCTCTCGCCGGTGG and SEQ ID NO: 39 is its corresponding translated 6 amino acid peptide Ser-Pro-Ser-Arg-Trp, which are supported at least at page 98, line 26. Finally, SEQ ID NO: 40 is the amino acid sequence FVLFHKIPLDG from Figure 1B, which is the trkB alternate C-terminal sequence, and SEQ ID NO: 41 is the amino acid sequence from Figure 2B which represents the trkC alternate C-terminal sequence.

As noted before, the SEQ ID NOS. in the specification have been amended to correspond to the submitted Sequence Listing. Additionally, on page 12 of the specification, various typographical errors have been corrected. Attached hereto are several pages indicating the exact changes made to the specification by the current amendment. The attached pages are captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE." On these pages additions are underlined and deletions are struck through. As indicated above, a replacement page 118 is also attached and is captioned "REPLACEMENT SHEET."

No new matter has been introduced by these amendments.

Sequence Rule Compliance

Along with the present Amendment Applicants file a Sequence Listing in paper copy and computer readable form, as well as a statement that the two versions are the same, and do not add new matter to the specification. The entry of the Sequence Listing, which Applicants' believe to

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REPLACEMENT SHEET

TABLE 1

<u>USE</u>	<u>trkA</u>	<u>trkB</u>	<u>TrkC</u>
Degenerate Sense		TGYGAYATHATGTGGYTNAARAC SEQ ID NO: 10	TGGATGCARYTNTGGCARCARCA SEQ ID NO: 11
Degenerate Anti		YTCRTCYYTNCRTAYTCRTT SEQ ID NO: 12	CCYTCYTGRARTAYTCNACGTG SEQ ID NO: 13
ECD insert Sense	CACGTCAACAACGGCAACTACA SEQ ID NO: 14	GGAAGGATGAGAAACAGATTCTGDC SEQ ID NO: 15	CATCAATGGCCACTTCCTCAAGG SEQ ID NO: 16
ECD insert Anti	AGGTGTTTCGTCCTTCTTCTCC SEQ ID NO: 17	GAGATGTGCCCGACCGTTGTATC SEQ ID NO: 18	CACAGTGATAGGAGGTGTGGGA SEQ ID NO: 19
TK insert Sense	GGATGTGGCTCCAGGCCCC SEQ ID NO: 20	GGGCAACCCGCCACGGAA SEQ ID NO: 21	ACGCCAGGCCAAGGGTGAG SEQ ID NO: 22
TK insert Anti	TAACCACTCCCAGCCCCTGG SEQ ID NO: 23	TTGGTGGCCTCCAGCGGCAG SEQ ID NO: 24	AATTCATGACCACCAGCCACCA SEQ ID NO: 25
Probes			
ECD sense	GCTCCTCGGGACTGCGATGC SEQ ID NO: 26	ATGTCGCCCTGGCCGAGGTGGCAT SEQ ID NO: 27	AAGCTCAACAGCCAGAACCTC SEQ ID NO: 28
ECD anti	CAGCTCTGTGAGGATCCAGCC SEQ ID NO: 29	CCGACCGGTTTATCAGTGAC SEQ ID NO: 30	ATGATCTTGGACTCCCGCAGAGG SEQ ID NO: 31
TK specific Sense		CTTGGCCAAGGCATCTCCGGT SEQ ID NO: 32	ATGTGCAGCACATTAAGAGGA SEQ ID NO: 33
TK specific Anti		TTATACACAGGCTTAAGCCATCCA SEQ ID NO: 34	AGGAGGCATCCAGCGAATG SEQ ID NO: 35

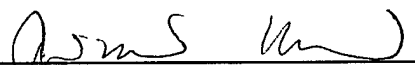
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be in full compliance with the requirements of 37 C.F.R. §§1.821 through 1.825, is respectfully requested. A copy of the "Notice the Comply" is returned with the present Amendment.

Respectfully submitted,

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Dated: July 11, 2001

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification

The paragraph beginning on page 12, line 4 has been amended as follows:

--**Figure 4. Summary of the splice forms seen in human and other mammalian trks.** Shown are schematic representations of the forms of the various trks arising from alternate slicing. Domains are after Schneider and Schweiger, supra. Data ~~for~~ is redrawn from the literature for rat trkA (Meakin, *et al.*, Proc. Natl. Acad., Sci. USA 89, 2374-2378 [1992], Barker *et al.*, J. Biol. Chem. 268, 15150-15157 [1993]), rat and mouse trkB (Klein, *et al.*, EMBO J. 8, 3701-3709 [1989]; Klein *et al.*, Cell 61, 647-656 [1990], Middlemas *et al.*, Mol. Cell. Biol. 11, 143-153 [1991]) and rat and pig trkC (Lamballe, *et al.*, Cell 66, 967-979 [1991]; Valenzuela *et al.*, Neuron 10, 963-974 [1993]; Tsoulfas, *et al.*, Neuron 10, 975-990 [1993]) Alternate forms of truncated rat trkC described by Valenzuela *et al.*, supra are omitted for clarity. The closed triangle in trkA extracellular region represents the optionally present peptide Ser-Pro-Ser-Arg-Trp (SEQ ID NO: 39) as described in the text. The half closed triangle in trkC extracellular region represents the optionally present 9 amino acid peptide ESTDNFILF (SEQ ID NO: 36) as described in the text. The smaller open triangle in trkC tyrosine kinase domain represents the optionally present 14 amino acid peptide LFNPSGNFCIWCE (SEQ ID NO: 37), and the larger open triangle in non-human trkC tyrosine kinase domain represents the optionally present 25 or 39 amino acid peptides.

The paragraph beginning on page 11, line 3 has been amended as follows:

Figure 1A and 1B shows the nucleotide sequence (SEQ ID NO: 1) and deduced amino acid sequence (SEQ ID NO: 2) of human trkB receptor. **A)** Figure 1A: The sequence of tyrosine kinase domain-containing trkB is shown (~~SEQ ID NO: 1~~) with potential N-linked glycosylation sites boxed, predicted transmembrane domain underlined, and tyrosine kinase domain flanked by arrows. The site of the splice giving rise to the truncated form is indicated by a single vertical line. **B)** Figure 1B: The sequence (SEQ ID NO: 40) of the alternately spliced truncated intracellular domain is shown. The amino acid sequence and the nucleotide sequence of the truncated form of human trkB receptor are attached as SEQ. ID. NOS: ~~6~~ 4 and ~~7~~ 3, respectively.

The paragraph beginning on page 11, line 15 has been amended as follows:

~~Figure 2 shows~~ Figures 2A and 2B show the nucleotide sequence (SEQ ID NO: 5) and the amino acid sequence (SEQ ID NO: 6) of human trkC receptor. A) Figure 2A: The sequence of tyrosine kinase containing trkC is shown (~~SEQ ID NO: 2~~) with potential N-linked glycosylation sites boxed, predicted transmembrane domain underlined, and tyrosine kinase domain flanked by arrows. The site of the splice giving rise to the truncated form is indicated by a single vertical line. The sequence of the potential inserts in the extracellular and tyrosine kinase domains are flanked by brackets. B) Figure 2B: The sequence (SEQ ID NO: 41) of the alternately spliced truncated intracellular domain is shown. The amino acid sequence and the nucleotide sequence of the truncated human trkC receptor are attached as SEQ ID NOS.: ~~4 and 5~~ 8 and 7.

The paragraph beginning on page 15, line 17 has been amended as follows:

Comparison of the amino acid sequences of full length human trkA, trkB and trkC receptors. The consensus sequences are boxed; the boundaries of the various domains are marked by vertical line (see SEQ ID NOS: ~~3, 1 and 2~~ 9, 2 and 6).

The paragraph beginning on page 98, line 16 has been amended as follows:

In the extracellular domain of human trkC, there was a possible deletion of nine amino acids compared to rat and pig trkC at a site near to that where the extracellular insert was described in rat and human trkA (Barker *et al.*, J. Biol. Chem. 268, 1510-15157 [1993]; Figure 2). PCR analysis of this region in human trkC showed only two bands, corresponding in length to that expected for the insert-containing and insert-deleted forms. PCR analysis of this region in human trkB showed no detectable length polymorphisms, but amplification using trkA specific primers did show two distinct bands which were cloned and sequenced. The potential nucleotide insert was TCTCCTTCTCGCCGGTGG (SEQ ID NO: ~~5~~ 38) at position 1297 coding for the identical peptide insert (SEQ ID NO: 39) previously described in rat and human trkA (Barker, *et al.*, supra).

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TABLE 1

<u>USE</u>	<u>trkA</u>	<u>trkB</u>	<u>TrkC</u>
Degenerate Sense		TGYGAYATHATGTGGYTNAARAC SEQ ID NO: 8 10	TGGATGCARYTNTGGCARCARCA SEQ ID NO: 9 11
Degenerate Anti		YTCRTCYYTTCRTAYTCRTT SEQ ID NO: 40 12	CCYTCYTGRARTAYTCNACGTG SEQ ID NO: 44 13
ECD insert Sense	CACGTCAACAACGGCAACTACA SEQ ID NO: 42 14	GGAAGGATGAGAAACAGATTTCTGDC SEQ ID NO: 43 15	CATCAATGGCCACTTCTCAAGG SEQ ID NO: 44 16
ECD insert Anti	AGGTGTTTCGTCCTTCTTCTCC SEQ ID NO: 45 17	GAGATGTGCCCCACCGGTTGTATC SEQ ID NO: 46 18	CACAGTGATAGGAGGTGTGGGA SEQ ID NO: 47 19
TK insert Sense	GGATGTGGCTCCAGGCCCC SEQ ID NO: 48 20	GGGCAACCCGCCACGGAA SEQ ID NO: 49 21	ACGCCAGGCCAAGGGTGAG SEQ ID NO: 50 22
TK insert Anti	TAACCACTCCAGCCCCTGG SEQ ID NO: 54 23	TTGGTGGCCTCCAGCGGCAG SEQ ID NO: 55 24	AATTCATGACCACCAGCCACCA SEQ ID NO: 56 25
Probes			
ECD sense	GCTCCTCGGGACTGCGATGC 24 SEQ ID NO: 26	ATGTCGCCCTGGCCGAGGTGGCAT 25 SEQ ID NO: 27	AAGCTCAACAGCCAGAACCTC 26 SEQ ID NO: 28
ECD anti	CAGCTCTGTGAGGATCCAGCC 27 SEQ ID NO: 29	CCGACCGGTTTATCAGTGAC 28 SEQ ID NO: 30	ATGATCTTGGACTCCCGCAGAGG 29 SEQ ID NO: 31
TK specific Sense		CTTGGCCAAGGCATCTCCGGT 30 SEQ ID NO: 32	ATGTGCAGCACATTAAGAGGA 34 SEQ ID NO: 33
TK specific Anti		TTATACACAGGCTTAAGCCATCCA 32 SEQ ID NO: 34	AGGAGGCATCCAGCGAATG 33 SEQ ID NO: 35